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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,769	07/21/2003	Birol Emir	109536.182	4223

26694 7590 11/22/2006

VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,769	EMIR ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7,10-13 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,10-13 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted September 26, 2006 wherein claims 1, 2, 8, and 9 are cancelled, claims 3-7 are amended, and new claims 10-23 are introduced. This application claims benefit of foreign application JP2002363139, filed December 13, 2002.

Claims 3-8 and 10-23 are pending in this application.

Claims 3-8 and 10-23 as amended are examined on the merits herein.

Applicant's amendment submitted September 26, 2006, with respect to the rejection of instant claims 5-8 under 35 USC 102(b) as being anticipated by Shua-Haim et al. has been fully considered and found persuasive to remove the rejection as the amendment adds the limitation, "Wherein severe Alzheimer's dementia is characterized by a score of 5 to 9 on the Mini-Mental State Examination," which is not taught by Shua-Haim et al. Therefore the rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-17 and 22-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment submitted September 26, 2006 with respect to new claims 14-17 and 22-23 has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for a method that results in an improvement the patient's score in the Mini-Mental State Examination, or in no change in the patient's score in said examination. Figure 1 discloses the effect of the treatment on the patient's score in the Severe Improvement Battery, which is a separate evaluation scale which is not the same as the MMSE. Table 2 discloses results based on improvement or deterioration as measured by the Clinician's Interview-Based Impression of Change scale, which is also different from the MMSE. Nowhere does the specification as originally filed disclose an effect or lack thereof of the claimed method on the patient's Mini-Mental State Examination score.

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc v. Mahurkar*, 19 USPQ 2d 1111 CAFC 1991, see also *In re Winkhaus,* 188 USPQ 129, CCPA 1975. Because Applicant's amendment necessitated this new ground of rejection, this rejection is made **FINAL**.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-7 and 10-23 are rejected under 35 U.S.C. 102(b) as being unpatentable over Feldman et al. (Reference included with PTO-1449) Feldman et al. discloses a study of the efficacy of donepezil for the treatment of moderate to severe Alzheimer's disease, characterized by a score of 5-17 on the Folstein Mini-Mental State Exam. (p. 614, left column, third paragraph) This range of scores overlaps with the limitation of claim eight, (a score of less than 10) and fully includes the limitations of claims 3, 4, and 9. (a score of 5-9) The dose administered to the patients was either 5 or 10 mg per day, (p. 614, left column, first paragraph) both of which fall within the dose limitations of claims 3, 6, 7, 11, 12, and 19-21. The dose was administered at 5 mg/day for 4 weeks, then increased to 10 mg per day, in a dosing regimen which was identical to that of instant claim 13. The method of Feldman et al. involves administering the same compound in the same dose to the same or similar patient population. Although it is not mentioned whether the patient's MMSE scores improved or remained constant during the treatment, as disclosed in instant claims 14-17, this outcome is considered to be inherent in the method of Feldman et al., as the steps disclosed in the reference are the same as in the instant claims, administering the same compound in the same amounts to the same subjects by the same mode of administration. See *Ex parte Novitski* 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that the claiming of a new use, new function, or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3c. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it relates to the claimed invention herein.

The claimed invention is thus anticipated by Feldman et al.

Response to Argument: Applicant's arguments, submitted September 26, 2006, with respect to the previous rejection of claims 3-9 on the grounds discussed above, have been fully considered and not found to be sufficient to remove the rejection. Applicant argues that the mean MMSE score of the patient population was outside of the claimed range. This argument is not convincing because anticipation of a range does not depend on whether the prior art discloses a range with a mean falling within the claimed range. According to MPEP 2131.03, a reference may anticipate a claimed range in the absence of specific examples falling within the range if the claimed range is disclosed with sufficient specificity to constitute an anticipation under the statute. In the instant case, a range was disclosed which included patients with severe to moderate AD. (MMSE scores 5-17 as opposed to 5-9 in the claimed invention) The focus of this study was on the treatment of **moderate to severe** AD using donepezil, as opposed to previous studies which had focused on **mild to moderate** AD. (p. 613, right column, second paragraph) Mild to moderate AD, as described by prior studies, included a range of MMSE scores of 10-26, (p. 618, left column, fourth paragraph), as opposed to moderate to severe AD which is disclosed as encompassing MMAS scores of 5-17, indicating that Feldman et al. was operating with the same definition of "moderate" and "severe" AD disclosed by Applicant. Feldman et al. specifically observes that the

disclosed results, "suggest that donepezil could be beneficial **for the symptomatic management of more advanced AD stages than those previously investigated**." (p. 618, left column, third paragraph) In other words, the reference specifically discloses the lower end of the subject population (those with severe AD) as being of special interest in that this population was not previously known to benefit from donepezil. Therefore, the subset of experimental subjects having severe AD, with a MMSE score of 5 to 9, are disclosed with sufficient specificity to anticipate the claimed invention.

For these reasons the rejection is maintained and made **FINAL**.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-7 and 10-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5100901. (herein referred to as '901).

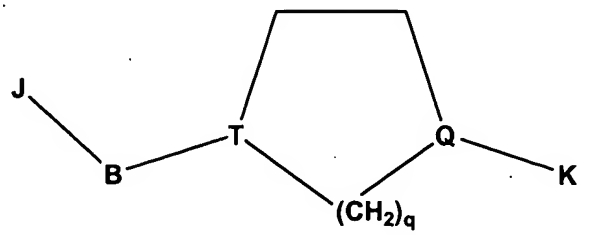

Figure 1 - The Compounds of claim 1 of US Patent 5100901

'901 discloses a therapeutic method involving a compound with a formula (XXV), shown in Figure 1 above. (and described in claim 1 of '901) The claim limitations of said claim include an instance in which J = (Indanonyl with two methoxy substituents), B = (CH_2), T = carbon, Q = nitrogen, K = phenylmethylene, and q = 2, which is identical to the compound 1-benzyl-4-(5,6-dimethoxy-1-indenone)2-yl-methylpiperidine, also known as donepezil, pictured below in figure 2 and described in instant claims 3-9. Although neither the claims nor the specification particularly point out donepezil as a specific embodiment of the claimed invention, a number of the specific examples shown in tables 4 and 9 are substantially structurally similar to donepezil. (For example, examples 28, 31, 33, and 35 in columns 47-50)

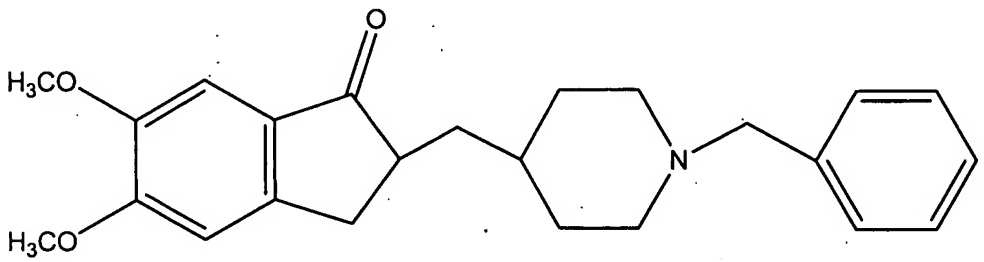

Figure 2- One instance of formula (XXV) of '901, also the compound of instant claims 3-9.

'901 defines the patient population as humans suffering from a disease accompanied by acetylcholinesterase activity. (claims 9-10) This is further limited to humans suffering from senile dementia in claim 9 and humans suffering from Alzheimer's disease in claim 10. Although it is not mentioned whether the patient's MMSE scores improved or remained constant during the treatment, as claimed in instant claims 14-17, the disclosed treatment comprises the same steps as the one claimed, and is thus expected to produce the same result. These claims do not

specifically claim a treatment of severe Alzheimer's disease characterized by a MMSE score of 5-9 by administering donepezil at a dosage of 3-10 mg, or 5 mg per day for 4 weeks followed by 10 mg per day as disclosed by new claim 13. However, the specification of '901 does disclose a dosage range of 1.0 to 300 mg per day, more preferably 1 to 100 mg per day. (Column 29, lines 41-43)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of '901 by developing a specific therapeutic method comprising administering to a human patient suffering from Alzheimer's disease characterized by a MMSE score of 5-9 by the administration of 5 or 10 mg per day of the specific compound donepezil.

One of ordinary skill in the art would have been motivated to modify the teaching of '901 in this way in order to optimally treat patients suffering from Alzheimer's disease. One of ordinary skill in the art would have reasonably expected success because the determination of exact details of patient population and dosage amounts is within the level of ordinary skill in the medical art. Furthermore, although the specific compound mentioned in the instant claims is not specifically recited in '901, it is included within the scope of the claimed generic structure (XXV), and is very similar to a number of specific embodiments pointed out in the specification of '901, thus leading one of ordinary skill in the art to reasonably conclude that it was useful in the methods of claims 9-10 of '901, based on the reasonable expectation that species that are very similar in structure usually have similar properties. See e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214.

Thus the invention taken as a whole is *prima facie* obvious

Claims 3-7 and 10-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 4895841. (herein referred to as '841)

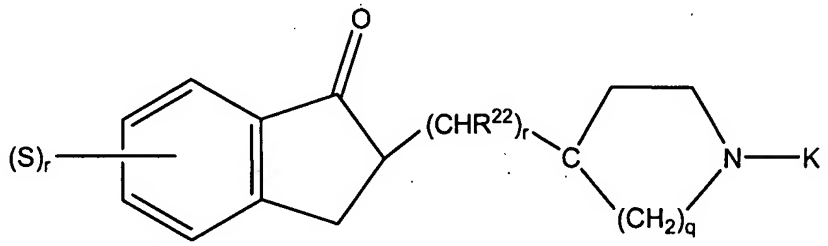

Figure 3 - The cyclic amine compounds of US Patent 4895841

'841 discloses a therapeutic method involving a compound with a formula (XXV), shown in Figure 3 above, and described in claim 1 of '841. (Claims 12-13) The claim limitations of said claim include an instance in which r = 1, K = phenylmethylene, S = methoxy, t = 2, q = 2, and R^{22} = H, which is identical to the compound 1-benzyl-4-(5,6-dimethoxy-1-indenone)2-yl-methylpiperidine, also known as donepezil, pictured below in figure 4 and described in instant claims 3-9. Although it is not mentioned whether the patient's MMSE scores improved or remained constant during the treatment, as claimed in instant claims 14-17, the disclosed treatment comprises the same steps as the one claimed, and is thus expected to produce the same result. Although neither the claims nor the specification of '841 particularly point out donepezil as a specific embodiment of the claimed invention, a number of the specific examples shown in tables 4 and 9 are substantially structurally similar to donepezil. (For example, examples 28, 31, 33, and 35 in columns 49-52)

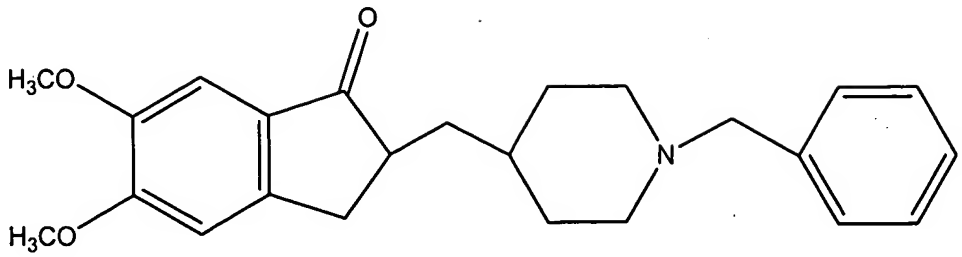

Figure 4- One instance of the formula of claim 1 of '841, also the compound of instant claims 3-9.

Claims 12-13 of '841 define the patient population as humans suffering from a disease accompanied by acetylcholinesterase activity. This is further limited to humans suffering from senile dementia in claim 12 and humans suffering from Alzheimer's disease in claim 13. These claims do not specifically claim a treatment of severe Alzheimer's disease characterized by a MMSE score of 5-9 by administering donepezil at a dosage of 3-10 mg, or 5 mg per day for 4 weeks followed by 10 mg per day as disclosed by new claim 13. However, the specification of '841 does disclose a dosage range of 1.0 to 300 mg per day, more preferably 1 to 100 mg per day. (Column 30, lines 24-26)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of '841 by developing a specific therapeutic method comprising administering to a human patient suffering from Alzheimer's disease characterized by a MMSE score of 5-9 by the administration of 5 or 10 mg per day of the specific compound donepezil.

One of ordinary skill in the art would have been motivated to modify the teaching of '841 in this way in order to optimally treat patients suffering from Alzheimer's disease. One of ordinary skill in the art would have reasonably expected success because the determination of exact details of patient population and dosage amounts is

within the level of ordinary skill in the medical art. Furthermore, although the specific compound mentioned in the instant claims is not specifically recited in '841, it is included within the scope of the claimed generic structure (XXV), and is very similar to a number of specific embodiments pointed out in the specification of '841, thus leading one of ordinary skill in the art to reasonably conclude that it was useful in the methods of claims 12-13 of '841, based on the reasonable expectation that species that are very similar in structure usually have similar properties. See e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214.

Therefore the invention taken as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3-7 and 10-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-10 of U.S. Patent No. 5100901. (herein referred to as '901) Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are an obvious subspecie of claims 8-10 of '901.

Claims 9-10 of '901 are directed to a therapeutic method involving a compound with a formula (XXV), shown in Figure 1 in the previous section. (and described in claim 1 of '901) The claim limitations of said claim include an instance in which J = (Indanonyl with two methoxy substituents), B = (CH_2), T = carbon, Q = nitrogen, K = phenylmethylene, and q = 2, which is identical to the compound 1-benzyl-4-(5,6-dimethoxy-1-indenone)2-yl-methylpiperidine, also known as donepezil, pictured in figure 2 in the previous section and described in instant claims 3-9. Although neither the claims nor the specification particularly point out donepezil as a specific embodiment of the claimed invention, a number of the specific examples shown in tables 4 and 9 are substantially structurally similar to donepezil. (For example, examples 28, 31, 33, and 35 in columns 47-50)

Claims 9-10 of '901 define the patient population as humans suffering from a disease accompanied by acetylcholinesterase activity. This is further limited to humans suffering from senile dementia in claim 9 and humans suffering from Alzheimer's disease in claim 10. Although it is not mentioned whether the patient's MMSE scores improved or remained constant during the treatment, as claimed in instant claims 14-17, the disclosed treatment comprises the same steps as the one claimed, and is thus

expected to produce the same result. These claims do not specifically claim a treatment of severe Alzheimer's disease characterized by a MMSE score of 5-9 by administering donepezil at a dosage of 5 or 10 mg, or 5 mg per day for 4 weeks followed by 10 mg per day as disclosed by new claim 13. However, the specification of '901 does disclose a dosage range of 1.0 to 300 mg per day, more preferably 1 to 100 mg per day. (Column 29, lines 41-43)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of '901 by developing a specific therapeutic method comprising administering to a human patient suffering from Alzheimer's disease characterized by a MMSE score of 5-9 by the administration of 3-10 mg per day of the specific compound donepezil.

One of ordinary skill in the art would have been motivated to modify the teaching of '901 in this way in order to optimally treat patients suffering from Alzheimer's disease. One of ordinary skill in the art would have reasonably expected success because the determination of exact details of patient population and dosage amounts is within the level of ordinary skill in the medical art. Furthermore, although the specific compound mentioned in the instant claims is not specifically recited in '901, it is included within the scope of the claimed generic structure (XXV), and is very similar to a number of specific embodiments pointed out in the specification of '901, thus leading one of ordinary skill in the art to reasonably conclude that it was useful in the methods of claims 9-10 of '901, based on the reasonable expectation that species that are very similar in structure

usually have similar properties. See e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214.

Claims 3-7, and 10-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-13 of U.S. Patent No. 4895841. (herein referred to as '841) Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are an obvious subspecie of claims 12-13 of '841.

Claims 12-13 of '841 are directed to a therapeutic method involving a compound with a formula (XXV), shown in Figure 3 in the previous section. (and described in claim 1 of '841) The claim limitations of said claim include an instance in which r = 1, K = phenylmethylene, S = methoxy, t = 2, q = 2, and R^{22} = H, which is identical to the compound 1-benzyl-4-(5,6-dimethoxy-1-indenone)2-yl-methylpiperidine, also known as donepezil, pictured in figure 4 in the previous section and described in instant claims 3-9. Although neither the claims nor the specification of '841 particularly point out donepezil as a specific embodiment of the claimed invention, a number of the specific examples shown in tables 4 and 9 are substantially structurally similar to donepezil. (For example, examples 28, 31, 33, and 35 in columns 49-52)

Claims 12-13 of '841 define the patient population as humans suffering from a disease accompanied by acetylcholinesterase activity. This is further limited to humans suffering from senile dementia in claim 12 and humans suffering from Alzheimer's disease in claim 13. Although it is not mentioned whether the patient's MMSE scores

improved or remained constant during the treatment, as claimed in instant claims 14-17, the disclosed treatment comprises the same steps as the one claimed, and is thus expected to produce the same result. These claims do not specifically claim a treatment of severe Alzheimer's disease characterized by a MMSE score of 5-9 by administering donepezil at a dosage of 5 or 10 mg, or 5 mg per day for 4 weeks followed by 10 mg per day as disclosed by new claim 13. However, the specification of '841 does disclose a dosage range of 1.0 to 300 mg per day, more preferably 1 to 100 mg per day. (Column 30, lines 24-26)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of '841 by developing a specific therapeutic method comprising administering to a human patient suffering from Alzheimer's disease characterized by a MMSE score of 5-9 by the administration of 3-10 mg per day of the specific compound donepezil.

One of ordinary skill in the art would have been motivated to modify the teaching of '841 in this way in order to optimally treat patients suffering from Alzheimer's disease. One of ordinary skill in the art would have reasonably expected success because the determination of exact details of patient population and dosage amounts is within the level of ordinary skill in the medical art. Furthermore, although the specific compound mentioned in the instant claims is not specifically recited in '841, it is included within the scope of the claimed generic structure (XXV), and is very similar to a number of specific embodiments pointed out in the specification of '841, thus leading one of ordinary skill in the art to reasonably conclude that it was useful in the methods of claims 12-13 of '841,

based on the reasonable expectation that species that are very similar in structure usually have similar properties. See e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214.

Response to Argument: Applicant's arguments, submitted September 26, 2006, with respect to the rejection of claims 3-9 under both 35 USC 103 and the judicially created doctrine of obviousness-type double patenting as being obvious over either of US patents 5100901 and 4895841, have been fully considered and not found to be persuasive to remove the rejection. Applicant argues that one of ordinary skill in the art would not consider acetylcholinesterase inhibitors such as donepezil to be useful for treating severe Alzheimer's dementia because severe Alzheimer's dementia has a different pathology than mild and moderate dementia. Essentially, as Alzheimer's disease progresses to severe dementia, changes in the brain occur which cannot be ameliorated by acetylcholinesterase inhibitors. Thus, it would not be expected that an acetylcholinesterase inhibitor would be a successful treatment. However, in order to reasonably be considered a successful treatment, a treatment does not have to successfully treat or ameliorate all symptoms of a disease, particularly in an incurable, invariably fatal condition such as Alzheimer's dementia. In particular, one of ordinary skill in the art would expect that the neural changes characteristic of mild and moderate Alzheimer's disease do not disappear in severe Alzheimer's dementia. Rather, they are accompanied by further abnormalities which are not responsive to acetylcholinesterase inhibition. (e.g. decrease in brain volume, loss of neural structure) Based on this consideration, it would be apparent to one of ordinary skill in the art that

acetylcholinesterase inhibitors would still produce an effect in severe Alzheimer's dementia, although the effect would be less significant in comparison to the magnitude of disability brought on by the additional and untreatable effects of severe dementia. Whether this effect would be sufficient to warrant continuing treatment past this point is a decision which would be made by one of ordinary skill in the art on consideration of the specific circumstances of each case. Therefore one of ordinary skill in the art would reasonably expect donepezil to be useful for treating severe Alzheimer's dementia. Thus the arguments are not found persuasive and these four rejections are made **FINAL**.

Summary

No claims are allowed in this application. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Eric Olson
Eric S. Olson
Patent Examiner
AU 1623
11/7/06

Anna Jiang
11/15/06
Supervisory Patent Examiner
AU 1623